PATENT

#8
2/15/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellants :	Robin R. Miles et al	Appeal No. :	
Serial No. :	09/737,542	Docket No. :	IL-10406
Filed :	December 14, 2000	Art Unit :	1641
For:	Impedance Measurements for Detecting Pathogens Attached to Antibodies	Examiner :	K. Padmanabhan

BRIEF ON APPEAL

Commissioner for Patents
Washington, D.C. 20231

Sir:

Appellant hereby appeals to the Board of Patent Appeals and Interferences from the decision dated October 10, 2001 of the Examiner finally rejecting Claims 10-21.

Real Parties in Interest

The real parties in interest are the Regents of the University of California and the United States of America as represented by the United States Department of

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Related Appeals and Interferences

Appellants know of no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

Status of the Claims

Claims 10-21 are presently in the Application. Claims 10-21 stand finally rejected. Thus, Claims 10-21 are now on appeal. A copy of the claims on appeal is presented in Appendex A.

Status of Amendments

No Amendment Under 37 CFR 1.116 has been filed. However, a Request for Reconsideration was filed on November 13, 2001. However, the seven(7) separate grounds of rejection were maintained as set forth in the Advisory Action mailed November 30, 2001.

Summary of Invention

The present invention is directed to the use of impedance measurements to detect the presence of pathogen attached to antibodies, and more particular to pathogens attached to antibody coated beads. Basically, the present invention replaces the prior optical detection approach with the detection of the attachment of antibodies to pathogens using the change of impedance between two electrodes as a way of making a less expensive pathogen detection system. The detection system or sensor of this invention, may for example, use patterned intedigitated electrodes on the surface of a fluid channel, with an AC or DC voltage applied across the

electrodes to produce a non-uniform electric field. Antibodies are immobilized on the surfaces of the electrodes and the impedance between the electrodes is measured. Following the passage of a sample fluid containing pathogens through the fluid channel and by the electrode surface, certain of the pathogens are attached to the immobilized antibodies, thereby causing a change in the impedance between the electrodes, which change of impedance provides a measurement by which the presence of the pathogens can be determined. To amplify the impedance change signal, antibody coated beads may be introduced which attached to the trapped pathogens causing a greater change in impedance between the electrodes. The pathogen sensor of this invention can be used, for example, in counter biological warfare detectors to detect the presence of pathogens, or in any antibody-based assay system.

Figure 1-7, a copy presented as Appendix B, illustrate embodiments of the invention. Figure 1 illustrates in cross-section a fluidic channel with patterned interdigitated electrodes formed on a surface of the channel with electric fields shown across the various legs of the interdigitated electrodes, with Figure 2 illustrating an enlarged view of the patterned interdigitated electrodes of Figure 1 with an AC power supply across the legs of the electrodes to produce the electric field of Figure 1. The embodiment of Figures 1 and 2 is described in detail on page 7 of Appellants' specification.

Since antibodies can be immobilized on a surface, the present invention utilizes surfaces of two spaced electrodes or two adjacent legs of patterned interdigitated electrodes as a surface on which the antibodies are immobilized, as illustrated in Figure 3 and described in detail on page 8 of Appellants' specification, the electrodes of Figure 3 being two of the adjacent legs of the interdigitated electrodes of Figure 1 and 2. The pathogen streaming by the electrode surfaces

attach to the immobilized antibodies, as seen in Figure 4, and thus changes the impedance between the two electrodes, which is measured, as by the sensor of Figure 7, to detect the presence of a pathogen. To amplify this impedance change signal, one or more beads coated with antibodies are introduced into the sample fluid flow, and the beads stick to the trapped pathogen as seen in Figure 5, and described on page 8 of the specification. The coated beads further add to the change in impedance between the two electrodes. The coated bead or beads can be moved in and out of the signal region using either electrophoretic, dielectrophoretic, magnetic, or pressure flow modes so that the bead or beads could be recycled. Beads bound to pathogen could be eluted and the surface reactivated. Also, a second set of electrodes could be placed beneath the first set to act as a reference signal, as shown in Figure 6, and described on page 8 of the specification. The sensor of Figure 7, and described on page 9 of the specification, is shown operatively connected to two electrodes, such as shown in Figures 3-6, but may be expanded to be connected between two adjacent legs of the interdigitated electrodes of Figure 2. The patterned interdigitated electrodes may be located on a surface of the fluidic channel, as shown in Figure 1, or can be located within the fluidic channel by use of spaced wires or suspended structures.

In the embodiments illustrated in Figures 3-5 and Figure 6, only two electrodes are shown for simplicity of illustration, and such are illustrated as electrodes or electrode fingers 20 and 18 of Figures 1 and 2. The electrodes can be

straight, as shown, or can be curved, with either uniform or variable widths or thickness.

Issues

1. Whether Claims 10, 12, 16, and 21 are anticipated by Kipling et al under 35 USC 102(b)?

2. Whether Claims 10, 12, 15-16, and 21 are anticipated by Stettler et al under 35 USC 102(b)?

3. Whether Claims 10, 12-13, 16, and 21 are anticipated by Clerc under 35 USC 102(b)?

4. Whether Claims 10-14, 16-19, and 21 are anticipated by Taylor et al under 35 USC 102(b)?

5. Whether Claims 10, 12-18, and 21 are anticipated by Vadgama et al under 35 USC 102(b)?

6. Whether Claims 10, 12-14, 16-18, and 21 are anticipated by Van Gerwen et al under 35 USC 102(b)?

7. Whether Claim 20 is obvious in view of either Taylor et al, Vadgama et al, or Van Gerwen et al under 35 USC 103(a)?

8. Whether a fluidic channel as known in the art means "any surface on which a fluid can travel?

9. Whether the "means for measuring impedance between said spaced electrodes" as set forth in Claim 20 is known in the art?

Grouping Of The Claims

Claim 10 sets forth "An apparatus for determining the trapping of pathogen by antibodies deposited in a fluidic channel", while Claim 16 sets forth "A sensor using impedance measurements to detect the presence of pathogens attached to antibodies", and thus are of significantly different scope and should not stand or fall together. Claims 11 and 13 set forth additional structural features than those of parent Claim 10 and thus should not stand or fall with the parent claim. Claim 20 sets forth structural features in addition to the features of parent Claim 16 and should not stand or fall with the parent claim.

Arguments

This is an appeal from the six (6) different rejections of Claims 10 and 16, along with various dependent claims under 35 USC 102 on each of Kipling et al, Stetter et al, Clerc, Taylor et al, Vadgama et al, and Van Gerwen et al, and the rejection of Claim 20 under 35 USC 103 as unpatentable over each of Taylor et al, Vadgama et al, and Van Gerwen et al. The rejections under 35 USC 102 as set forth in paragraphs 2-7 of the Final Rejection are a word-for-word repeat of the rejections set forth in paragraphs 13-18 of the Office Action mailed 6/20/01.

Issue #1

Claims 10, 12, 16, and 21 are rejected under 35 USC 102(b) as anticipated by Kipling et al. Claim 10, for example, sets forth a "fluidic channel", and Claim 16 sets forth "at least one microchannel". Kipling et al fails to teach a "fluidic channel" or a

"microchannel". The Examiner contends that a "fluidic channel" is "any surface on which a fluid can travel", which would include a flat surface of glass etc. Fluidic and microfluidic devices, as known in the art, include channels or microchannel (grooves in one or more surfaces, along which sample fluid, etc., passes. A flat surface does not constitute a fluidic channel or microchannel. Thus, Kipling et al fails to teach each feature recited in Claims 10 and 16, for example, and thus fails to support a rejection of these claims under 35 USC 102, and the rejection should be reversed.

Issues #2-6

In an effort to reduce the record, the 35 USC 102(b) rejections set forth in paragraphs 3-7 of the Final Rejection are being argued simultaneously since each rejection includes parent Claims 10 and 16. Claim 10 sets forth:

"an apparatus for determining the trapping of pathogen by antibodies deposited in a fluidic channel", comprising:

1. "a fluidic channel having at least one pair of spaced electrodes therein";
2. "antibodies located on said spaced electrodes";
3. "means for producing an electric field across said spaced electrodes", and
4. "an impedance sensor for measuring impedance between said spaced electrodes".

Claim 16 sets forth

> "A sensor using impedance measurements to detect the presence of pathogens attached to antibodies", comprising:

1. A microfluidic device having at least one microchannel therein",

2. "spaced electrodes located on a surface of said microchannel",

3. "antibodies located on said spaced electrodes",

4. "an AC or DC power supply for producing an electric filed across said spaced electrodes", and

5. "means for measuring impedance between said spaced electrodes.

The Examiner was called upon in Appellants' Amendment filed 9/24/01 to specifically identify where each claimed feature is taught in each reference since Appellants were unable to locate such specific teachings, and the Examiner's generalized statements did not lead Appellants to an understanding of exactly where the four(4) features of Claim 10 and the five(5) features of Claim 16 are found in each of these references. The Examiner merely repeated the various grounds of rejection. Where in the reference Taylor et al is found a specific teaching of the features of Claim 11? Where in each of these references is there taught that "said at least one pair of spaced electrodes is located on a surface of said fluidic channel (Claim 12)? Where are the features of Claim 13 and/or 14 found in each Clerc, Taylor et al, Vadgama et al and Van Gerwen et al? Where are the features of Claims 17 and 18 taught by each of the references Taylor et al, Vadgama et al, and Van Gerwen et al? Where are the features of Claim 19 found in Taylor et al?

The Examiner's "interpretation" of the term "fluidic channel" is most interesting, the Examiner stating that:

> "a fluidic channel is interpreted as meaning any surface on which a fluid can travel."

Under the Examiner's interpretation, a "fluidic channel" may constitute any flat surface" on which a fluid can travel. Are not claim terms to be read in light of the art to which they relate? Here, a "fluidic channel" is recognized in the art as a groove, cutaway, etc. on a surface of a member through which a fluid flows, not merely a flat surface as interpreted by the Examiner.

Aside from the issue of the meaning of "a fluidic channel", Claim 10 as outlined above sets forth three(3) additional features not taught by any of these five applied references. The Examiner has failed to point out where any of these three (3) additional features are taught, but merely states that the references "do indeed disclose either one or a combination" of features. To support a rejection under 35 USC 102, each applied reference must teach each feature recited in the claims so rejected. Also, the Examiner states on page 6 of the Final Rejection that "the references anticipated or render obvious the claims against which they were applied". There are no 35 USC 103 rejections of these claims on these references, and therefore the "render obvious" statement is an incorrect response. Thus, the rejection of these claims under 35 USC 102 on any of the five(5) applied references is improper and should be reversed.

Issue #7

Claim 20 is rejected under 35 USC 103(a) as unpatentable over each of Taylor *et al*, WO 98/19153, and WO 97/21094. Claim 20 depends from Claim 16 and includes all the structural features of the parent claim. As pointed out above, each of these references fail to teach the features of parent Claim 16. The Examiner admits that these references fail to teach the features of Claim 20, but contends that such are

obvious. If such "means for measuring impedance" is obvious as contented by the Examiner, such should be taught in the prior art, and thus the Examiner should cited prior art which teaches the features as set forth in Claim 20. Thus, this rejection should be reversed.

Issue #8

While this issue has been discussed above, it is submitted that a "fluidic channel" (Claim 10) or "at least one microchannel" (Claim 16) does not define "any surface on which a fluid can travel" as stated by the Examiner. Such terms do not include any flat surface as would be included by the Examiner's stated interpretation. Thus, it is submitted that the Examiner's interpretation is incorrected and should be clarified by the Board.

Issue #9

If the "means for measuring impedance" as set forth in Claim 20 is known in the art, then the Examiner should cite prior art to teach the specific components set forth in Claim 20. The mere holding that such "means" is obvious without prior art teachings is improper and should be reversed.

Basis for Grouping of Claims

Claim 10 sets forth "An apparatus for determining the trapping of pathogen by antibodies in a fluidic channel", the apparatus comprising four (4) components, while Claim 16 set forth "A sensor using impedance measurements to detect the presence of pathogens attached to antibodies", the sensor comprising five (5) components. None of the six references applied against Claims 10 and 16 teach each of the four (4)

components of Claim 10 or the five (5) components of Claim 16 as required to support a rejection thereof under 35 USC 102, as pointed out above in detail. Further, Claim 10 recites "a fluidic channel", and Claim 16 sets forth "at least one microchannel", neither of which are taught by each of the applied six (6) references. Further, the Examiner's interpretation that "a fluidic channel" means "any surface on which a fluid can travel" is incorrect, since terms of claims are to be considered in light of the state of the art, and a "fluidic channel" or a "microchannel" is known in the art as defining a groove, etc., along which fluid passes. For example, Webster's New Collegiate Dictionary defines "fluidic" as:

> "of, relating to, or being a device...that depends for operation on the pressures and flows of a fluid in precisely shaped channel" (underlining added).

This same Dictionary defines a "channel" as:

> "a long gutter, groove, or furrow".

Thus, the Examiner's definition of a "fluidic channel", which would include any flat surface is clearly inconsistent with established definitions of the term. As to the term "microchannel" of Claim 16, the above referenced Dictionary defines "micro" as:

> "small: minute", "abnormally small", "of or relating to a small area."

Thus, the "microchannel" of Claim 16 would not be "any surface on which a fluid can travel" as stated by the Examiner.

Claim 11, which depends from Claim 10, adds to the "apparatus" of parent Claim 10, adds three (3) additional features; namely:

1. "at least one pair of reference electrodes...";

2. "an insulator...", and

3. "said reference electrodes being electrically connected to said impedance sensor."

According to the rejections under 35 USC 102, these three (3) features, plus the four (4) features of parent Claim 10, are taught by Taylor et al. It is noted that the rejection of Claim 11 is totally silent as to the three (3) features of this claim.

Claim 13, which depends from Claim 12 and Claim 10 sets forth that:

> "said at least one pair of spaced electrodes comprises a plurality of adjacent pairs of spaced electrodes."

This claim is rejected under 35 USC 102 based on the teachings of each of Clerc, Taylor et al, Vadgama et al, and Van Gerwen et al. It is noted that there is no discussion in any of these rejections of the features of Claim 13, although the last sentence in the rejection on Clerc, states that: "The apparatus may also comprise a second pair of spaced electrodes (Col. 10). However, a "second pair of spaced electrodes" does not teach the claimed "plurality of adjacent pairs of spaced electrodes" as set forth in Claim 13. This is a 35 USC 102 rejection and thus the reference applied must teach each feature of the claim so rejected.

Claim 20, which depends from Claim 16, adds to the features of parent Claim 16, the following:

1. "a plurality of signal generators",

2. "a current sensor connected to at least one electrode",

3. "a plurality of amplifier/mixer assemblies connected in parallel to said current sensor",

4. "said signal generators each being connected to one of said amplifier/mixer assemblies", and

5. "one of said signal generators being additionally connected to another of said spaced electrodes".

Thus, for each of the references, Taylor et al, Vadgama et al, and Van Gerwen et al to teach or suggest, either expressly or impliedly, as required under 35 USC 103, these references must teach or suggest the ten (10) features of Claim 20 which include the five (5) features of parent Claim 16. However, the Examiner admits that "none of these references teach the use of a plurality of signal generators, a current sensor attached to an electrode, and a plurality of mixer/amplifier assemblies", but contends that such would be "prima facie obvious" to incorporate such features in these references. Where does the obviousness come from, except from Appellants' disclosure? Here is a clear case of an improper attempt to provide references with features taught only by Appellants' disclosure. Such hindsight reconstruction has been held to be impermissible under 35 USC 103.

Thus, Claims 10, 11, 13, and 16 are not taught by the references applied under 35 USC 102, and Claim 20 is not taught or suggested by any of the references applied thereagainst under 35 USC 103. Thus, the rejection of these claims is improper and should be reversed.

Conclusion

It is submitted that the Examiner's rejections under 35 USC 102 based on the six (6) references applied, and the 35 USC 103 rejection based on the three (3) references applied, are each improper and should be reversed.

Respectfully submitted,

Dated: 2-5-02

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Enclosures:
Appendix A
Appendix B

APPENDIX A
S.N. 09/737,542
Claims on Appeal

10. An apparatus for determining the trapping of pathogen by antibodies deposited in a fluidic channel, comprising:

a fluidic channel having at least one pair of spaced electrodes therein,

antibodies located on said spaced electrodes,

means for producing an electric field across said spaced electrodes, and

an impedance sensor for measuring impedance between said spaced electrodes.

11. The apparatus of Claim 10, additionally including at least one pair of reference electrodes located in spaced relation to said at least one pair of spaced electrodes, an insulator located between said reference electrodes and said pair of spaced electrodes, said reference electrodes being electrically connected to said impedance sensor.

12. The apparatus of Claim 10, wherein said at least one pair of spaced electrodes is located on a surface of said fluidic channel.

13. The apparatus of Claim 12, wherein said at least one pair of spaced electrodes comprises a plurality of adjacent pairs of spaced electrodes.

14. The apparatus of Claim 13, wherein said plurality of adjacent pairs of spaced electrodes are formed by adjacent fingers of an interdigitated electrode located on the surface of said fluidic channel.

15. The apparatus of Claim 10, wherein said means comprises an AC power supply.

16. A sensor using impedance measurements to detect the presence of pathogens attached to antibodies, comprising:

a microfluidic device having at least one microchannel therein,

spaced electrodes located on a surface of said microchannel,

antibodies located on said spaced electrodes,

an AC or DC power supply for producing an electric field across said spaced electrodes, and

means for measuring impedance between said spaced electrodes.

17. The sensor of Claim 16, wherein said spaced electrodes comprise fingers of an interdigitated electrode formed on said surface of said microchannel.

18. The sensor of Claim 17, wherein said interdigitated electrode includes fingers forming a plurality of adjacent pairs of spaced electrodes.

19. The sensor of Claim 15, additionally including reference electrodes located in insulated relation to said spaced electrodes and electrically connected to said means for measuring impedance.

20. The sensor of Claim 16, wherein said means for measuring impedance between said spaced electrodes includes a plurality of signal generators, a current sensor connected to at least one electrode, a plurality of amplifier/mixer assemblies connected in parallel to said current sensor, said signal generators each being

connected to one of said amplifier/mixer assemblies, and one of said signal generators being additionally connected to another of said spaced electrodes.

21. The sensor of Claim 1, wherein the at least one pair of spaced electrodes is formed within the fluidic channel.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	Robin R. Miles, et al.	Docket No. :	IL-10406
Serial No. :	09/737,542	Art Unit :	1641
Filed :	December 14, 2000	Examiner	K. Padmanabhan
For :	Impedance Measurements for Detecting Pathogens Attached to Antibodies		

Commissioner for Patents
Washington, D.C. 20231

EXPRESS MAIL CERTIFICATE

"Express Mail" label number EL534310305US

Date of Deposit 2-5-02

I hereby certify that the following *attached* correspondence, **all in triplicate,** comprising:

1. Transmittal of Brief on Appeal (2 pages) (in triplicate)
2. Brief of Appeal (14 pages) (in triplicate)
3. Appendix A (Claims on Appeal) (3 pages) (in triplicate)
4. Appendix B (Drawings) (3 sheets) (in triplicate)
5. Return postcard (original only)

is being deposited with the United States Postal Service "Express Mail Post Office to addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box: AF, Commissioner for Patents, Washington D.C. 20231.

April Masluk
(Type or print name of person mailing paper)

April Masluk
(Signature of person mailing paper or fee)

02-11-02

$AF

PATENT 1641

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	Robin R. Miles, et al.	Docket No. :	IL-10406
Serial No. :	09/737,542	Art Unit :	1641
Filed :	December 14, 2000	Examiner	K. Padmanabhan
For :	Impedance Measurements for Detecting Pathogens Attached to Antibodies		

TRANSMITTAL OF BRIEF ON APPEAL
(PATENT APPLICATION - 37 CFR 192)

Transmitted herewith in **triplicate** is the **BRIEF ON APPEAL** in this application with respect to the Notice of Appeal filed on December 13, 2001.

The item(s) checked below are appropriate:

1. **STATUS OF APPLICANT**
   This application is on behalf of
   - ❑ other than a small entity.
   - ■ a small entity.
     A verified statement
     - ❑ is attached
     - ■ already filed.

2. **FEE FOR FILING APPEAL BRIEF**
   Pursuant to 37 CFR 1.17(e) the fee for filing the Appeal Brief is:
   - ■ small entity $160.00
   - ❑ other than a small entity $320.00

   Appeal Brief fee due **$160.00**

CERTIFICATE OF MAILING/TRANSMISSION (37 CFR 1.8a)

I hereby certify that this correspondence is, on the date shown below, being:

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April Masluk
(Type or print name of person mailing paper)

April Masluk
(Signature of person mailing paper)

3. **EXTENSION OF TIME**

☐ Applicant petitions for an extension of time under 37 CFR 1.136

Calculation of extension fee (37 CFR 1.17(a)-(d)):

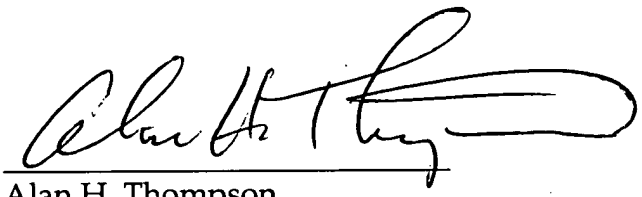
	Total months requested	Fee for other than small entity	Fee for small entity
☐	one month	$110.00	$55.00
☐	two month	$380.00	$190.00
☐	three month	$870.00	$435.00
☐	four month	$1,360.00	$680.00
☐	five month	$1,850.00	$925.00
		Fee	**$000.00**

4. **FEE PAYMENT**

■ Charge Account No. 12-0695 in the amount of **$160.00**.

■ **Charge Account No. 12-0695 for any additional extension and/or fee required or credit for any excess fee paid.**

Date: 2-5-02



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